

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference <b>00786-608WO1</b>	<b>FOR FURTHER ACTION</b>	See item 4 below
International application No. <b>PCT/US2004/041300</b>	International filing date ( <i>day/month/year</i> ) <b>09 December 2004 (09.12.2004)</b>	Priority date ( <i>day/month/year</i> ) <b>10 December 2003 (10.12.2003)</b>
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant <b>THE GENERAL HOSPITAL CORPORATION</b>		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).
2. This REPORT consists of a total of 4 sheets, including this cover sheet.  
  
In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.
3. This report contains indications relating to the following items:

<input checked="" type="checkbox"/>	Box No. I	Basis of the report
<input type="checkbox"/>	Box No. II	Priority
<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/>	Box No. IV	Lack of unity of invention
<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/>	Box No. VI	Certain documents cited
<input type="checkbox"/>	Box No. VII	Certain defects in the international application
<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. +41 22 740 14 35	Date of issuance of this report <b>12 June 2006 (12.06.2006)</b>  Authorized officer  <div style="text-align: center; font-weight: bold; font-size: 1.2em;">Beate Giffo-Schmitt</div>  Telephone No. +41 22 338 87 20
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# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

REC'D 03 JUN 2005

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To:  
J. PETER FASSE  
FISH & RICHARDSON P.C.  
225 FRANKLIN STREET  
BOSTON, MA 02110-2804

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference 00786-608WO1		Date of mailing (day/month/year) <b>01 JUN 2005</b>
<b>FOR FURTHER ACTION</b> See paragraph 2 below		
International application No. PCT/US04/41300	International filing date (day/month/year) 09 December 2004 (09.12.2004)	Priority date (day/month/year) 10 December 2003 (10.12.2003)
International Patent Classification (IPC) or both national classification and IPC IPC(7): C12Q 1/26 and US Cl.: 435/25		
Applicant THE GENERAL HOSPITAL CORPORATION		

**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I      Basis of the opinion
- ☐ Box No. II      Priority
- ☐ Box No. III      Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV      Lack of unity of invention
- ☒ Box No. V      Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI      Certain documents cited
- ☐ Box No. VII      Certain defects in the international application
- ☐ Box No. VIII      Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Marcela M Cordero Garcia Telephone No. (571) 272-1600
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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/41300

**Box No. I Basis of this opinion**

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/US04/41300

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>1-52</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>8-14, 27-35, 37-38 and 43-51</u>	YES
	Claims <u>1-7, 15-26, 36, 39-42 and 52</u>	NO
Industrial applicability (IA)	Claims <u>1-52</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-7, 15-26, 36, 39-42 and 52 lack an inventive step under PCT Article 33(3) as being obvious over Josephson et al (WO 02/098364) alone.

Josephson et al. beneficially teach a composition comprising at least two nanoparticle conjugates each nanoparticle conjugate comprising:

a magnetic nanoparticle.

at least one substrate moiety, in which each substrate moiety is linked to the nanoparticle; wherein

when the target polypeptide is absent, the nanoparticle conjugates are essentially monodisperse in a liquid; and

when the target polypeptide is present, the nanoparticle conjugates self-assemble into one or more nanoparticle conjugate clusters through the formation of intermolecular linkages between the chemically modified substrate moieties (see entire document, e.g., page 2, lines 22-24, page 4, lines 16-22, page 7, lines 3-14, page 15, lines 18-28 and claims).

Josephson et al. do not specifically teach substrate moieties that are chemically modified when the conjugate interacts with a target enzyme.

Chemical modification of the substrate moieties when the conjugate interacts with a target enzyme is deemed as intrinsic because formation of clusters shifts the electronic configuration (and hence the chemical properties) of the moieties involved. It would have been obvious to one of ordinary skill in the art at the time the invention was made to adjust particular conventional working conditions within such compositions (e.g., using specifically enzymes as target biomolecules and/or forming covalent or non-covalent clusters) based upon the overall beneficial teachings provided by Josephson et al. These types of adjustments are deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan.

Thus, the invention as a whole is prima facie obvious over the reference, especially in the absence of evidence to the contrary.

Claims 8-14, 27-35, 37-38, 43-51 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the limitations in these claims.

Claims 1-52 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.